08-07-0341

1653

Docket 17324CIP1

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: DONOVAN	**Examiner: Chih Min Kam**
Serial Number: 09/810,601	**Art Unit: 1653**
Filed: March 15, 2001	**Confirmation No.: 9283**
For: COMPOSITIONS AND METHODS FOR TREATING GONADOTROPHIN RELATED ILLNESSES	**Irvine, California**

TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Please find enclosed with regard to the above-identified pending U.S. patent application: (1) an 11 page response to the April 21, 2003 Office Action in the above-identified patent application; (2) a return postcard, and; (3) this 2 page Transmittal Letter.

Applicant respectfully petitions for a one month extension of time to respond to the Office Action.

The fee has been calculated as shown below:

CLAIMS AS FILED

	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA	RATE	ADDITIONAL FEE
Total Claims	8	2	= 6 x	$18	= $108.00
Independent Claims	2	1	= 1 x	$84	= $84.00
If application has been amended to contain multiple dependent claim(s), then add			No	$280	= $0.00
Time Extension Fees:			1 mth	$110.00	= $110.00
Terminal Disclaimer Fee:					=$0.00
TOTAL ADDITIONAL FEE FOR THIS AMENDMENT					**$302.00**

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The Commissioner is hereby authorized to charge fees under 37 CFR 1.16 and 1.17 (associated with petition fees or excess claim fees) which may be required, or credit any overpayment to Deposit Account No. 01-0885. A duplicate copy of this sheet is enclosed.

Date: August 5, 2003

Stephen Donovan
Registration Number 33,433

Allergan, Inc.,
Legal Department
2525 Dupont Drive, T2-7H
Irvine, CA 92612
Telephone: 714 246 4026 Fax: 714 246 4249

CERTIFICATE OF EXPRESS MAIL UNDER 37 C.F.R. § 1.10

I hereby certify that this Transmittal Letter, the Response to Office Action and the documents referred to as enclosed therein are being deposited with the United States Postal Service on this date **August 5, 2003** in an envelope as "Express Mail Post Office to Addressee" Mailing Label number EV295682965US addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450

Susan Bartholomew
Name of person mailing paper

Date: August 5, 2003

Signature of person signing paper

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial Number: 09/810,601	**Art Unit: 1653**
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For: Compositions and Methods for Treating Gonadotrophin Related Illnesses	**Irvine, California**

RESPONSE TO OFFICE ACTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

This response amends claim 22, cancels claim 23 and adds new claims 24-30 (see pages 10-11 of this response).

I. The Office Action

The April 21, 2003 non-final office action (the "Office Action") in this application:

1. objected to claim 23;

2. rejected claims 22 and 23 under 35 U.S.C. section 112, first paragraph;

3. rejected claims 22 and 23 under 35 U.S.C. section 112, second paragraph, and;

6. rejected claims 22-23 under 35 U.S.C. section 103(a) as being unpatentable over Nett (U.S. patent 5,707,964) in view of Johnson (U.S. patent 5,939,070).

Applicant responds to the Office Action as follows.

II. Objection to Claim 23

The Office Action objected to claim 23. Claim 23 has been cancelled and claim 22 has been limited to treatment of the specific diseases breast cancer, prostate cancer, pancreatic cancer, and endometrial cancer.
Hence, the basis for the objection has been removed.

III. Rejection Claims 22 and 23 under 35 U.S.C. section 112(1)

The Office Action rejected claims 22 and 23 under 35 U.S.C. §112, first paragraph. The Office Action states on page four that the specification is "...enabling for a method of treating a specific gonadotrophin related disease such as prostate cancer, breast cancer or endometrial cancer in a mammal comprising administering an agent of a botulinum toxin (or a butyricum toxin or a tetani toxin) component covalently coupled to GnRH or a functional GnRH analog, wherein the toxin component is the LH_N."

The claims have been amended to such an enabling claim scope. Therefore the rejection should be withdrawn.

IV. Rejection Claims 22 and 23 under 35 U.S.C. section 112(2)

The Office Action rejected claims 22 and 23 under 35 U.S.C. §112, second paragraph.

The rejection is based on: (1) an omitted step of the outcome of the treatment, and; (2) use of the term "a fragment thereof", variants thereof" or "a modified heavy chain".

The claims have been amended to address both bases for the rejection. Hence, the rejection should be withdrawn.

V. New Claims 24-30

New claim 24 is supported by at least original claim 2.

New claim 25 is supported by at least original claim 3.

New claim 26 is supported by at least original claim 4.

New claim 27 is supported by at least original claim 6

New claim 28 is supported by at least original claim 7.

New claim 29 is supported by at least original claims 2, 3 and 6.

New claim 30 is supported by at least original claim 4 .

No new matter or any new issues is introduced by any of new claims 24-30.

VI. Rejection of Claims 22-23 Under Section 103(a)

The Office Action rejected claims 22-23 under 35 U.S.C. §103(a) as being unpatentable over Nett (U.S. patent 5,707,964) in view of Johnson (U.S. patent 5,939,070).

Nett discloses a conjugate of GnRH with particular bacterial or plant toxin domains. Johnson discloses hybrid botulinum toxins. The Office Action states that it would have been obvious to combine the GnRH component of Nett with the botulinum toxin of Johnson to thereby obtain the claimed invention.

Respectfully, the rejection is in error and should be withdrawn.

Nett does not disclose any botulinum toxins. Nett discloses only GnRH conjugated to toxins which are cytotoxic. In other words, all the toxin-GnRH conjugates of Nett act to kill their target cells: See e.g. in Nett: "destroy the gonadotrophs" (Abstract); "ablating those pituitary cells" (column 5, lines 44-45); "However, if conjugated to one of applicant's GNRH analogs, the resulting molecule can interact with GnRH receptors and gain entry into the pituitary cell, thereby preventing protein synthesis and ultimately causing the desired effect - cell death" (column 10, lines 2-7); "serve to permanently destroy a subpopulation of the anterior pituitary cells" (column 12, lines 4-6); "a specific killing effect of the toxin conjugate" (column 20, lines 18-19), and; "by destroying the gonadotrophs" (column 22, line 17) '

Contrarily, it is well known that botulinum toxin acts by reversibly inhibiting release of neurotransmitter into a synaptic junction. See e.g. Johnson at column 3, lines 64-67. Thus, internalization of the light chain of a botulinum toxin by a target cell results in a reversible inhibition of particular intracellular secretory mechanisms. See e.g. the present specification as page 6, lines 18-23. It is well known that botulinum toxin is not a cytotoxin. That is the effect of a botulinum toxin upon a cell is only to temporarily

inhibit release of certain secretory vesicles from the target cell. That is why the effect of botulinum toxin typically wears off after 3-4 months. See the present specification at page 15, lines 3-5. Note that Examples 2 and 4, in this application require repeat treatment because the effect of a botulinum toxin (including as a botulinum toxin-GnRH conjugate) can wear off.

It is noteworthy that Nett discloses a number of suitable bacterial toxins but is silent as to any of the botulinum toxins, which are also bacterial toxins.

Since Nett discloses only cytotoxic GnRH toxin conjugates and Johnson discloses only hybrid botulinum toxins, Nett can not be combined with Johnson to produce the claimed invention. In other words, a combination of Nett and Johnson discloses, teaches and suggests only cytotoxic toxin conjugates, but the claims in the present application are all limited to botulinum toxin conjugates which are not cytotoxic compounds. Note pages 22, lines 31-32 of the present specification: "..the effects(s) of the light chain component is/are reversible." Clearly, the effects of botulinum toxin are reversible because botulinum toxin is not cytotoxic.

For these reasons the rejection should be withdrawn.

VII. Conclusion

All issues raised by the Office Action have been addressed. Reexamination, reconsideration and allowance of claims 22 and 24-30 is requested.

Respectfully Submitted,

Date: August 5, 2003

Stephen Donovan
Registration Number 33,433

Please direct all correspondence to:

Stephen Donovan
Allergan, Inc.
2525 Dupont Drive, T2 7H
Irvine, California 92612

Telephone: 714 246 4026
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Susan Bartholomew
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